

# Biological Ethics

## The Fantastic Future

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WE EASTERNERS ARE well aware of the Western (or should I say Californian) tendency to simplify problems. Naturally the dangers and inherent falseness of some simplifications are evident, and on these occasions I eschew them like the true Easterner that I am not; but for this discussion I propose to use the Californian viewpoint. Simplification is absolutely essential when one attempts to discuss so complex a topic as biological ethics.

In this theoretical essay I will restrict myself to discussing biological ethics in relation to the "improvement" and continued existence of healthy and happy individual humans on this earth. The effect of humans on all levels of plants and animals will be minimized, except as these effects in turn affect humans. No attempt will be made to pay homage to the many important civic and religious mores of our times. The name of the game is not humanity, but the individual human.

### About Us

Humans have evolved into amazingly complex organisms with the power to cause radical changes in their environment; this is their most unique characteristic and also the reason that they must assume the greatest burden of responsibility of all creation. Other organisms either adapted to a changing environment by a process of genetic evolution, or perished. But man, in changing his environment to suit his capricious tastes, can develop new "tinker toys" to streak through the air leaving huge trails of waste, or ravage his environment of desirable and perishable plants and animals and minerals,

all with an unbelievable recklessness. His skilled chemists provide ever more powerful compounds which may cause unanticipated havoc in remote areas or to seemingly unrelated organisms. The placid polar bear in his icy fastness is unaware that his fat, too, contains DDT. Compared with his animal neighbors, man has been amazingly destructive, and further he has taken no sustained interest in his effect upon his descendants. To be a completely responsible social animal he should not allow *any* accumulation of artificial waste products, whether they are burned, sunk into subterranean wells, or exhausted into the atmosphere or the surface waters. Gaseous, liquid, and solid wastes provide quantitative evidence of this failure of man's social responsibility. Thus wild tracts and polemics about social and economic problems are to a great extent unnecessary; we can measure our problems by our litter.

### Us

Equally acute are the personal problems facing individual physicians and scientists. Reckless use of scientific findings which in themselves are not inherently good or evil, plus the overwhelming desire to know and the possibility of extending life, has created conflict between the scientist's action and the mores of society. The recent advent of heart transplants merely dramatized the fragility of social rules which had already been distorted by the potentials of medical science. Some of this conflict may be temporarily resolved by careful deliberation; the solutions may be valid for a short time — until a new discovery again disrupts social stability.

There is need for a new kind of judiciary and advisory group with omnisocial interests. So far we

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are seeking wisdom about biological ethics by balancing our established mores with the statements of our most heroic and charismatic figure of the moment, be he a young surgeon or an aging philosopher. For example, we are beginning to investigate the ethical problems of transplantation, from the viewpoint of deciding in what part of the body reside the most unique characteristics of an individual — his identity. Most people would not deny that the therapeutic or accidental loss of arms or legs deprives the central nervous system of pleasurable stimuli and robs the body of important neuromuscular functions for survival and maintenance of health in the nervous system. Nevertheless, major amputations—even hemicorporectomy and quadriplegia—do not, from a social standpoint, significantly alter the essence of a patient's personality and identity. Our recognition of this fact is reflected in our strenuous and often commendable efforts to keep such individuals alive.

Transplanted kidneys do not change the identity of the recipients, and it is unlikely that more permanent allogenic transplants of legs, hearts, lungs and other internal organs will cause any more concern of this kind. Indeed, to press the point further, an individual might have all his body parts replaced and still retain the individuality of his genetic packet and his characteristic interaction with the environment—unless the higher centers of his brain were affected. In other words, if Joe receives a new heart, new lungs, new arms, and new legs, to himself and his family he is still Joe, even though he is now a more fragile, allosymbiotic Joe.

Thus the generalization can be made that the unique characteristics of an individual reside in the higher centers. (For convenience only, I will use the term *cerebral cortex*.) Even altering the brain with chemical agents will at some point have to be considered a change in identity. When it becomes possible to preserve and transplant the human brain — an unlikely possibility now but one which will some day have to be faced — new ethical problems will arise. When routine brain transplants are possible, there is little doubt society will conclude that identity is inherent in the brain—not in the fingerprints.

If one accepts the cerebral cortex as the seat of individual identity, the moment of death is easier to define, and one of our knottiest current problems becomes a little easier to handle. One noted author-physician asked whether anyone would bury a per-

son whose heart was still beating. From the point of view of society, the answer must be no; but from the scientist's point of view, the response might just as ethically be yes, *if* the brain were functionless. Cessation of the vital signs is a meaningful criterion of death only in that the static heart and quiet lungs reflect the impending or actual death of the brain. There is no more reason to preserve someone with a viable heart and a dead brain than there is to preserve someone whose heart and brain have long since ceased to function, but whose skin lives on.

## The Future Us

These problems are spectacular and immediate; but there are problems of biological ethics more remote, yet of even greater significance for the individual and human society. Problems concerning the moment of death and the identity of a transplantation recipient can be investigated by hearings and legislation, and present decisions can be modified by judicial processes and public opinions.<sup>1</sup>

Less tangible problems are equally pressing and more far-reaching in importance, but these cannot be solved by decree or even by public consensus. As an example of one such problem, I refer to our recently developed ability to grow normal human cells in culture. This example will include some scientific jargon and complexities which may tempt the reader to skip to the summary. But read on; it is that temptation to wish for instant understanding which is part of science's social problem.

When human cancer cells were successfully cultured, society did not feel threatened, and little public interest was aroused. There was more interest when a series of investigators began to grow seemingly normal human fibroblasts. Then the question began to arise, "Are human cells really people?"

The question was asked more urgently when the possibility of maintaining an infinite life of normal human cultured cells became a reality.<sup>2</sup> When normal human cells were first cultured, some scientists concluded that these cultured normal fibroblasts were mortal and could not survive more than 50 or 60 generations. (Generation is used to denote the average time for a culture population to double and thus requires division of the culture into new flasks.) Other scientists disputed Hayflick's claim, but still experience tended to support the thesis of a finite life span of normal cells.

Now in this laboratory we have been successful

in culturing seemingly normal human lymphoblasts from over two hundred individuals; the cell lines have remained in culture for more than two years or over 600 generations without showing any loss of viability or normality. Moreover, we can now assure the infinite life of these cell lines either by continuous culture or by freezing and maintaining them at  $-196^{\circ}\text{C}$ , then reculturing the stored cells.

Recognition of the biological and philosophical aspects of this exciting development became evident from the number of people who offered themselves for leukapheresis, and from the interest of these volunteers in whether *their* cells were growing well. One high school student was intensely disappointed when his cell line had to be discontinued because of contamination; and his feelings reflected his deep sense of personal loss. (He was reassured when he found out that we had kept samples of his cells in the cell bank, from which they might be restored at any time.)

Identity of the individuals from whom certain cell lines have been derived is of interest not only to the individual, but also to scientists. In theory, it is desirable to preserve the anonymity of the donor, but emotionally and practically it is much easier to identify cultures by name than by initials or code numbers. Thus RPMI #5287 and RPMI #6237 are commonly referred to as Moore and Flic cells despite attempts to suppress the identities. Even the use of initials or code numbers has not preserved the anonymity of the donors. But one shocking episode proved to us that all cells *should* be coded immediately. A staff member volunteered for leukapheresis and joyfully asked us every few weeks how *her* cells were doing. A permanent cell line was established — with an abnormal karyotype. I decided that this fearful news should be withheld from the childless donor, since on the basis of our present incomplete knowledge we cannot say whether or not the extra minute chromosome is harmful.

In view of the personal nature of these cultured cells, it seems reasonable to obtain an informed consent from the donors unless the cells will be kept for a limited time. For example, a donor might seriously object to his cells being used for venereal disease research, especially if the cells were identified. Most persons, fortunately, consent readily and are pleased by the possibility that their cells may be used in laboratories around the world. Moreover, one can foresee circumstances in which the existence of a cell line might be life-saving to

the donor. For example, if an individual developed a severe lymphopenia, transfusion of his own normal cultured lymphoid cells might constitute useful therapy.

Even if only certain favored cell lines are preserved or continuously cultured, the storage problems will become very troublesome under our present methods. Maintaining 12,000 ampules in liquid nitrogen units and keeping records of them are already a financial burden.

But what of the future implications of growing theoretical people in the laboratory and discarding some in the sink and changing others with drugs and x-ray? Someday, it will be possible to store cells safely for centuries in a satellite orbiting in the intense cold of outer space. (Space vehicles may be unreliable, but they surpass by far the reliability of laboratory freezers.)

Who is to decide whose cells lines will live and whose will be discontinued? It is more than an academic question, since sooner or later it may become possible to grow humans from their cells. The plant physiologists already are able to culture single cells of certain plants and trees until, after several intermediate stages involving changes in culture media, hormones and environmental conditions, a new adult plant develops. One might have dreams or nightmares of someone by-passing decades of research and of circumvention of critical biological principles — to biopsy his favorite movie star or political leader, and grow a dozen of them in the laboratory! Then again, there is some scientific evidence that the genetic packet of a somatic cell could be inserted into an enucleated egg cell to initiate normal differentiation. This intermediate method emphasizes the possible ethical and moral problems of human cell research.

As a concluding jolt, may I state that this recent flurry of interest over the substitution of the nucleus of an intestinal cell into a de-nucleated, fertilized frog egg caused many responses about the legislation of *future* research. But I can think of three ways in which we should be able to produce viable humans from cells right now—so we'd better hurry before the future turns into history, and mankind is shattered in the process.

### Legal Problems of "Us Cells"

There are other, more immediate problems associated with the culture of cells from apparently normal individuals. Suppose the cells from a seemingly normal person are found to be abnormal; should

the donor be told that he faces an increased risk of producing abnormal progeny? If the answer is yes, then we may have an obligation to screen all individuals — for their sake if not for society. As noted previously, we have already been faced with such a problem.

The clash between progress in biological research and the stability of human ethics is epitomized by a chromosome anomaly, the XYY syndrome.<sup>3</sup> Probably throughout the centuries some odd, tall, perhaps mentally retarded men have committed arson and sexual crimes and exhibited other antisocial behavior. They were treated like other men by the courts until it was found that they had an extra Y chromosome. Thus study of the contents of a single human cell may alter the status of an individual before the court and affect his rights. In some trials involving XYY individuals, verdicts have been altered, and in several notorious cases awaiting trial the Y chromosome may be the chief witness for the defense! The real importance of the XYY syndrome cannot be evaluated until we can determine how many unidentified persons with reasonable social adjustments have the XYY syndrome. Further, other men may have a double dose of the critical genes of second Y chromosome *without* having the extra chromosome. Must they be punished for the lack of a separate packaging of their genes?

The sort of genetic research made possible by the availability of cultured cells may be vitally important to many individuals. For example, it may become possible to correct the expression of genetic defects by several techniques which are now or will be available. The decision as to who will direct this genetic engineering, and in what circumstances it should take place, are problems which must be faced. Even now we can imagine the conflict between good and evil motives that could be wrought by the potential use of these techniques.

### The Legislative Problem of Us

The exposition of several aspects of biological research which will sooner or later require specific social, legislative and judicial decisions is not difficult. The problem of assigning responsibility is much more complex. Several important principles are involved; for example, should the judiciary establish new ethical guides? My personal reply is no — their role should be confined to the review of existing legislation. It is evident to any scientist who has tried to provide scientific testimony in court that the rigid rules of examination and cross-

examination and the inability of the jury to keep notes and clarify testimony by direct access to the witnesses may lead to horrendous errors. (I will refrain from commenting on the errors that might be made by aged jurists over-reacting and under-reacting in a vain effort to demonstrate their attunement with the times.) In the case of judgments based upon the presence of an extra Y chromosome, it is likely that equally severe genetic disorders which have no perceptible relationship to civil obedience may not be reflected in a gross change in size or shape of a chromosome — let alone the deletion or addition of an entire structure. Each chromosome probably has from ten to forty thousand genes or more; if individuals are treated uniformly on the basis of the number 46, or the size of the *wrapping* of their gene-bundles, then other individuals with abnormal gene patterns but no recognizable chromosome defects run the risk of injustice in the courts.

A second important principle is the responsibility of the State to clarify a point of biological ethics, once it is raised. In the present example a few scientists interested in genetics or chromosome structure are pursuing their work without, as far as I know, any additional support or urgency except that of the "will to know." Just a few weeks ago we accomplished, to my knowledge for the first time, the establishment of permanent human cell lines from patients with the XXY and XYY syndromes. My colleagues in government expressed scientific curiosity; but otherwise their social interest in this achievement was disheartening. In the circumstances, society should have the right to demand that a special effort be made to clarify the pertinent information so that the legislative and judicial branches of government will act on the basis of the best information available.

The problem is one of timing or of fact. Society must choose to study and regulate theoretical ideas, wait for tangible, new accomplishments, or, as now, delay until someone drops a really big bomb, grubs out a heart or performs some other act which usurps the public's attention.

Now that I have posed several complex problems, I should assume partial responsibility for suggesting solutions. It seems evident that good or bad, or good *and* bad legislative assemblies which are temporarily responsive to their society must have the responsibility for establishing changes in laws affecting biological ethics. It is the responsibility of scientists to keep them informed. The

perennial plea of the legislator for information engenders a feeling of hopelessness when the scientist checks his file of form letters which probably were dictated by a legislator's secretary's assistant. But how then can the facts be gathered, reviewed, and presented in such a way that they will penetrate the people-static which engulfs every legislator? It should not be necessary to produce an "over-kill" event (such as the heart transplants) in order to stimulate action.

Senator Walter F. Mondale (Minnesota) has suggested that a presidential commission undertake studies of the legal, social, and ethical implications of scientific research. An advisory committee to the Congress should be a more effective method of presenting information than holding multiple hearings by congressional committees on subjects of personal, political or categorical importance. Further, hearings which may be attended by only a chairman and one or two sleepy Congressmen are not the epitome of brain-to-brain communication. Contrary to today's fashion, I suggest that the advisory commission not include "consumers" since the consumers will be represented by Congress. Restricting the commission to scientists with interests ranging from animals, vegetables and minerals to the social sciences would aid in limiting its membership to ten or twelve. It would seem

wise to limit appointments by the President to a maximum of six years. (If I dared, I would suggest an age limit of 50 so that it would not become a refuge for retired Deans.)

I am well aware of historical efforts to restrict ideas and thus, in many instances, immortalize them. The commission must consider theory but act on fact. The success of such a group will depend upon the speed with which evaluations of the relative benefits and dangers of drugs, artificial viruses, hybrid cells, psychedelic drugs, radiation sources, and so on, in a broad sense can be accomplished and effective action begun. The commission should not be a substitute for existing surveillance and regulatory units which are needed for everyday problems but for those innovations which may, while converting the future into history, threaten or seriously alter or shatter mankind.

In summary, recent events have provided unchallengeable evidence of a need for a scientific advisory commission to consider the ethical and social aspects of new research findings for us and future mankind.

#### REFERENCES

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#### A WAY TO GET A URINE SPECIMEN FROM A GIRL BABY

"According to a pediatrician I know, the best way to get a urine specimen from a female infant is by capitalizing on one of her natural reflexes — involuntary urination at the time one of her heels is punctured for a blood sample. After cleansing the region of the external urinary meatus, he has one nurse hold the child's legs apart and another hold a container. At the moment the heel is punctured, the infant will usually urinate; and the nurse, holding the labia apart with gloved hands, can collect a clean midstream specimen."

—JOHN C. SHERRIS, M.B., M.D., Seattle

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